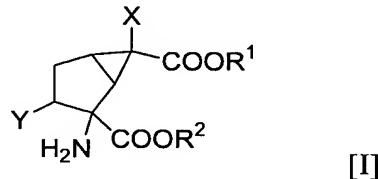


AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [I]



[wherein R¹ and R² are the same or different, and each represents a hydrogen atom, a C₁₋₁₀alkyl group, a phenyl group, a naphthyl group, a C₁₋₁₀alkyl group substituted by one or two phenyl groups, a C₂₋₁₀alkenyl group, a C₂₋₁₀alkynyl group, a hydroxylC₂₋₁₀alkyl group, a C₁₋₁₀alkoxycarbonylC₁₋₁₀alkyl group, an aminoC₂₋₁₀alkyl group or a C₁₋₁₀alkoxyC₁₋₁₀alkyl group;

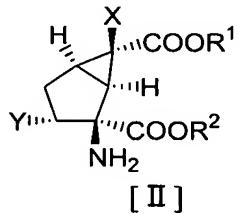
X represents a hydrogen atom or a fluorine atom;

Y represents an amino group, -SR³, -S(O)_nR⁷, -SCHR³R⁴, -S(O)_nCHR³R⁴, -NHCHR³R⁴, -N(CHR³R⁴)(CHR⁵R⁶), -NHCOR³ or -OCOR⁷ (wherein R³, R⁴, R⁵ and R⁶ are the same or different, and each represents a hydrogen atom, a C₁₋₁₀alkyl group, a phenyl group, a naphthyl group, a naphthyl group substituted by one to seven halogen atoms or a heteroaromatic group, or represents "a phenyl group substituted by one to five substituents

selected from a group consisting of a halogen atom, a phenyl group, a C₁₋₁₀alkyl group, a C₁₋₁₀alkoxy group and a trifluoromethyl group”;

R^7 represents a C_{1-10} alkyl group, a phenyl group, a naphthyl group, a naphthyl group substituted by one to seven halogen atoms or a heteroaromatic group, or represents “a phenyl group substituted by one to five substituents selected from a group consisting of a halogen atom, a phenyl group, a C_{1-10} alkyl group, a C_{1-10} alkoxy group and a trifluoromethyl group”; and n represents integer 1 or 2].

2. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II]



[Wherein R¹ and R² are the same or different, and each represents a hydrogen atom, a C₁₋₁₀alkyl group, a phenyl group, a naphthyl group, a C₁₋₁₀alkyl group substituted by one or two phenyl groups, a C₂₋₁₀alkenyl group, a C₂₋₁₀alkynyl group, a hydroxylC₂₋₁₀alkyl group, a C₁₋₁₀alkoxycarbonylC₁₋₁₀alkyl group, an aminoC₂₋₁₀alkyl group or a C₁₋₁₀alkoxyC₁₋₁₀alkyl group;

X represents a hydrogen atom or a fluorine atom;

Y represents an amino group, $-\text{SR}^3$, $-\text{S(O)}_n\text{R}^7$, $-\text{SCHR}^3\text{R}^4$, $-\text{S(O)}_n\text{CHR}^3\text{R}^4$, $-\text{NHCHR}^3\text{R}^4$, $-\text{N}(\text{CHR}^3\text{R}^4)(\text{CHR}^5\text{R}^6)$, $-\text{NHCOR}^3$ or $-\text{OCOR}^7$ (wherein R^3 , R^4 , R^5 and R^6 are

the same or different, and each represents a hydrogen atom, a C₁₋₁₀alkyl group, a phenyl group, a naphthyl group, a naphthyl group substituted by one to seven halogen atoms or a hetroaromatic group, or represents “a phenyl group substituted by one to five substituents selected from a group consisting of a halogen atom, a phenyl group, a C₁₋₁₀alkyl group, a C₁₋₁₀alkoxy group and a trifluoromethyl group”;

R⁷ represents a C₁₋₁₀alkyl group, a phenyl group, a naphthyl group, a naphthyl group substituted by one to seven halogen atoms or a hetroaromatic group or represents “a phenyl group substituted by one to five substituents selected from a group consisting of a halogen atom, a phenyl group, a C₁₋₁₀alkyl group, a C₁₋₁₀alkoxy group and a trifluoromethyl group”; and n represents integer 1 or 2].

3. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R² represents a hydrogen atom.

4. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R¹ and R² each represents a hydrogen atom.

5. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R¹ and R² each represents a hydrogen atom; and X represents a fluorine atom.

6. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R¹ and R² each represents a hydrogen atom; and

X represents a hydrogen atom.

7. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R¹ and R² each represents a hydrogen atom;

X represents a fluorine atom; and

Y represents -SR³ (-SR³ is the same as mentioned above).

8. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R¹ and R² each represents a hydrogen atom;

X represents a fluorine atom; and

Y represents -S(O)_nR⁷ (-S(O)_nR⁷ is the same as mentioned above).

9. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R¹ and R² each represents a hydrogen atom;

X represents a fluorine atom; and

Y represents -SCHR³R⁴ (-SCHR³R⁴ is the same as mentioned above).

10. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R¹ and R² each represents a hydrogen atom;

X represents a fluorine atom; and

Y represents -S(O)_nCHR³R⁴ (-S(O)_nCHR³R⁴ is the same as described above).

11. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R¹ and R² each represents a hydrogen atom; X represents a fluorine atom; and

Y represents -NHCHR³R⁴ (-NHCHR³R⁴ is the same as mentioned above).

12. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R¹ and R² each represents a hydrogen atom; X represents a fluorine atom; and

Y represents -N(CHR³R⁴)(CHR⁵R⁶) (-N(CHR³R⁴)(CHR⁵R⁶) is the same as mentioned above).

13. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R¹ and R² each represents a hydrogen atom; X represents a fluorine atom; and

Y represents -NHCOR³ (-NHCOR³ is the same as mentioned above).

14. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R¹ and R² each represents a hydrogen atom; X represents a fluorine atom; and

Y represents -OCOR⁷ (-OCOR⁷ is the same as mentioned above).

15. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R¹ and R² each represents a hydrogen atom; X represents a hydrogen atom; and Y represents -SR³ (-SR³ is the same as mentioned above).

16. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R¹ and R² each represents a hydrogen atom; X represents a hydrogen atom; and Y represents -S(O)_nR⁷ (-S(O)_nR⁷ is the same as mentioned above).

17. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R¹ and R² each represents a hydrogen atom; X represents a hydrogen atom; and Y represents -SCHR³R⁴ (-SCHR³R⁴ is the same as mentioned above).

18. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R¹ and R² each represents a hydrogen atom; X represents a hydrogen atom; and Y represents -S(O)_nCHR³R⁴ (-S(O)_nCHR³R⁴ is the same as mentioned above).

19. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R¹ and R² each represents a hydrogen atom;

X represents a hydrogen atom; and

Y represents $-\text{NHCHR}^3\text{R}^4$ ($-\text{NHCHR}^3\text{R}^4$ is the same as mentioned above).

20. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;

X represents a hydrogen atom; and

Y represents $-\text{N}(\text{CHR}^3\text{R}^4)(\text{CHR}^5\text{R}^6)$ ($-\text{N}(\text{CHR}^3\text{R}^4)(\text{CHR}^5\text{R}^6)$ is the same as mentioned above).

21. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by formula [II], wherein R^1 and R^2 each represents a hydrogen atom;

X represents a hydrogen atom; and

Y represents $-\text{NHCOR}^3$ ($-\text{NHCOR}^3$ is the same as mentioned above).

22. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, such a compound of formula [II] being:

(1R,2S,3R,5R,6R)-2-amino-3-(thiophene-2-ylmethylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(2-phenylbenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(4-methoxybenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(4-fluorobenzylsulfanyl)-6-fluorobicyclo [3.1.0]

hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(4-t-butylbenzylsulfanyl)-6-fluorobicyclo [3.1.0]

hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(3-trifluoromethylbenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(1-bromo-naphthalene-2-ylmethylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfinyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfonyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorophenylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(3-chloro-2,6-difluorobenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(propylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;

(1R,2S,3R,5R,6R)-2-amino-3-(1-phenyl-ethylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;
(1R,2S,3R,5R,6R)-2-amino-3-[bis-(4-fluorophenyl)methylsulfanyl]-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;
(1R,2R,3R,5R,6R)-2,3-diamino-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;
(1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylamino)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;
(1R,2R,3R,5R,6R)-2-amino-3-[N,N-(3,4-dichlorobenzyl)methylamino]-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid;
(1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzoylamino)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid; or
(1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzoyloxy)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid.

23. (original): A 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to claim 2, a pharmaceutically acceptable salt thereof or a hydrate thereof, such a compound of formula [II] being:

(1R,2R,3R,5R,6R)-2,3-diamino-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;
(1R,2S,3R,5R,6R)-2-amino-3-(thiophene-2-ylmethylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;
(1R,2S,3R,5R,6R)-2-amino-3-(2-phenylbenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(4-methoxybenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(4-fluorobenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(4-t-butylbenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3-trifluoromethylbenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(1-bromo-naphthalene-2-ylmethylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid 2-benzyl ester 6-ethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfinyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfonyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorophenylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3-chloro-2,6-difluorobenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(propylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(1-phenyl-ethylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-[bis-(4-fluorophenyl)methylsulfanyl]-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylamino)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2R,3R,5R,6R)-2-amino-3-[N,N-(3,4-dichlorobenzyl)methylamino]-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzoylamino)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid diethyl ester;

(1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzoyloxy)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid 2-benzyl ester 6-ethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid 2-ethyl ester;

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid 6-isobutyl ester; or

(1R,2S,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzylsulfanyl)-6-fluorobicyclo [3.1.0] hexane-2,6-dicarboxylic acid 6-benzyl ester.

24. (currently amended): A drug comprising the 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative according to ~~any one of claims 1 to 23~~claim 1, the pharmaceutically acceptable salt thereof or the hydrate thereof as an active ingredient.

U.S. National Stage Entry of
PCT/JP2004/009384
-filed June 25, 2004

Q92272

25. (original): The drug according to claim 24 wherein the drug is a Group II
metabotropic glutamate receptor antagonist.